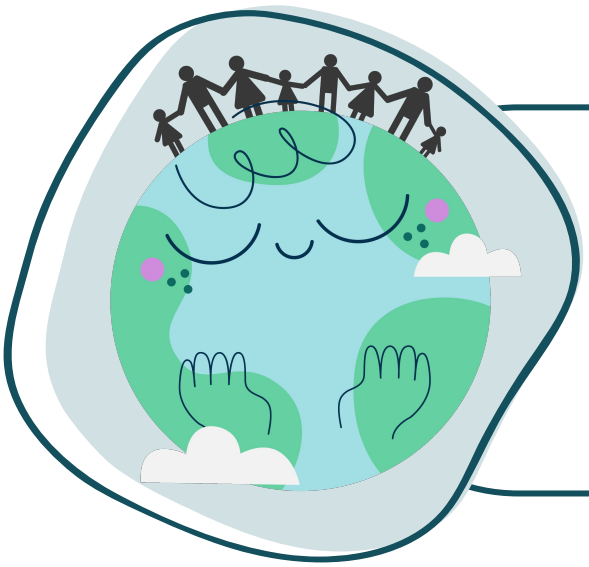
Reviewed By
Noura Alturki
Jehad Alorainy



Malaria

Objectives

- Understand the epidemiology and global burden of malaria
- Understand the epidemiology and risk factors related to Malaria in KSA
- Understand the cycle of infection of malaria
- Define modes of transmission, clinical features, risk factors, community diagnosis and treatment for malaria
- Enlist the factors responsible for antimalarial drug resistance
- Understand the role and measures taken by WHO to combat the burden of Malaria globally
- Enlist the global measures of prevention and elimination for Malaria
- **OSCE**

You can check the references at the end of the lecture if interested

Color Index

- Main text
- Males slides
- Females slides
- Doctor notes
- Important
- Textbook
- Golden notes
- Extra

Editing File

Malaria

- "Malaria is a life threatening febrile illness caused by infection with the protozoan parasite, Plasmodium. It is transmitted to humans by **the bite of the female Anopheles mosquito**[1]" (Public Health England 2013).

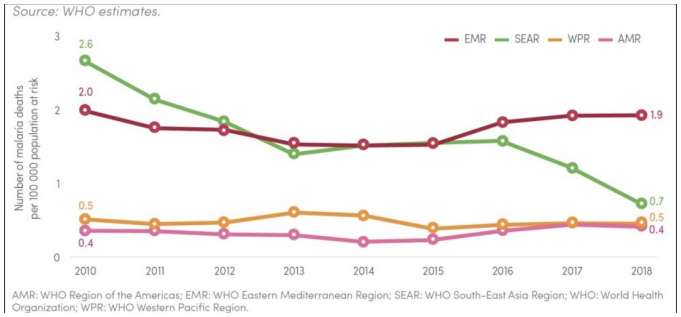
A typical attack comprises **three** distinct stages: cold stage, hot stage and sweating stage

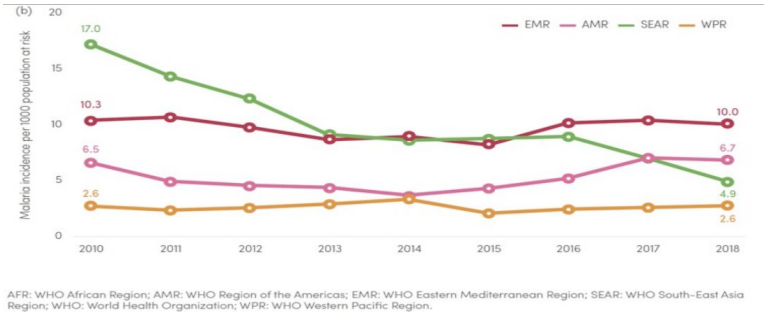
- **COLD STAGE:** The onset is with **lassitude**, **headache**, **nausea** and **chilly sensation** followed in an hour or so by **rigors**. The temperature **rises rapidly to 39-41°C.** Headache is often severe and commonly there is **vomiting**. In early part of this stage, skin feels cold; later it becomes hot. Parasites are usually demonstrable in the blood. The pulse is rapid and may be weak. This stage lasts for 15 mins -1 hour.
- **HOT STAGE:** The patient feels **burning hot and casts off his clothes.** The skin is **hot and dry to touch**. **Headache is intense** but **nausea commonly diminishes.** The pulse is full and respiration rapid. This stage lasts for 2 to 6 hours.
- **SWEATING STAGE:** Fever comes down with profuse sweating. The **temperature drops rapidly** to normal and **skin is cool and moist.** The pulse rate becomes **slower**, patient feels relieved and often falls asleep. This stage lasts for 2-4 hours

Epidemiology

- Malaria is globally one of the most important public health issues, predominantly affecting **young children** (Especially those who are less than 5 years) and **pregnant women.**
- In **2019**, there were 229 million cases and, 409,000 deaths caused by malaria worldwide (WHO 2020)
  - **67% of deaths were in children aged less than five years.**
  - **94% of cases and deaths occurred in Africa**[2]**.**
- Multidrug resistance is prevalent in many areas around the world[3], particularly in **South East Asia** (**Cambodia, Thailand,** Brunei, Burma (Myanmar), Timor-Leste, Indonesia, Laos, Malaysia, Philippines, Singapore and Vietnam.)(Kirwan 2006)

Regional trends and comparisons[4]





Red line: Middle East
Green line: South East Asia
Pink line: Region of the Americas (middle & South)
Orange: Western Pacific Region

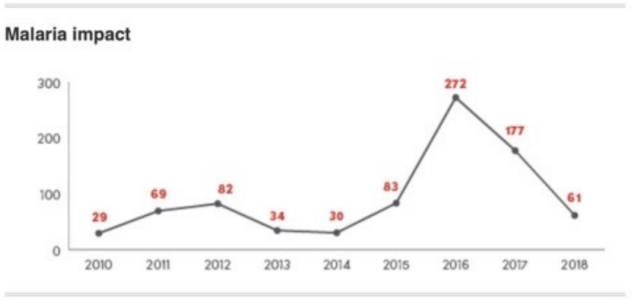
In the last 4-5 years, the incidence in the middle east is increasing causing an increase in the number of deaths.

1: Life threatening if not treated properly
2: There's always a risk of reintroduction to other countries
3: Like Saudi is chloroquine resistant
4: Why are the cases increasing ? Usually it's political reasons (like wars) more than health reasons. Poverty, war, etc can increase the chance of disease incidence and this will also cause the death percentages to increase

Malaria

Epidemiology in Saudi Arabia

- Dominant species in indigenous cases: **P. Falciparum** (93%), mainly transmitted by **Anopheles Arabiensis** (MOH 2019; WHO 2019)
- In 2018, number of confirmed cases was 2711, of which:
  - 2650 (97.7%) were either **imported** or **introduced**.
  - only 61 cases were **indigenous.**
- **Zero indigenous deaths** from 2010 to 2018.



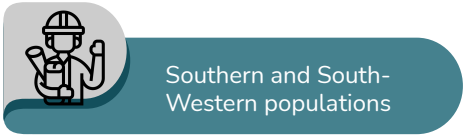
Source: *World malaria report 2019*

How malaria shaped history? The Doctor said this isn't from the objectives

- African v Native American slaves.
- In Africa, Europeans settlers preferred unfavourable environment to Anopheles.
- The unconquerable Rome and noxious fume "mal'aria".
- Around 1630, in Peru, missionaries found natives ingesting powdered bark of cinchona tree.
- Europeans learnt how to extract quinine, grow the cinchona and produce drugs.

High-risk populations in KSA

- **Imported** cases which represent (97%) of all cases (WHO 2019):
  - **Migrants**[1] (e.g., undocumented workers from Yemen and its neighbouring countries).
  - **Pilgrims** from endemic countries.
- **Indigenous** cases:
  - Southern and South-Western populations (**Jazan and Aseer**[2]) in coastal areas, lowlands and mountains due to seasonal anomalies (i.e., unusual high annual rainfall)



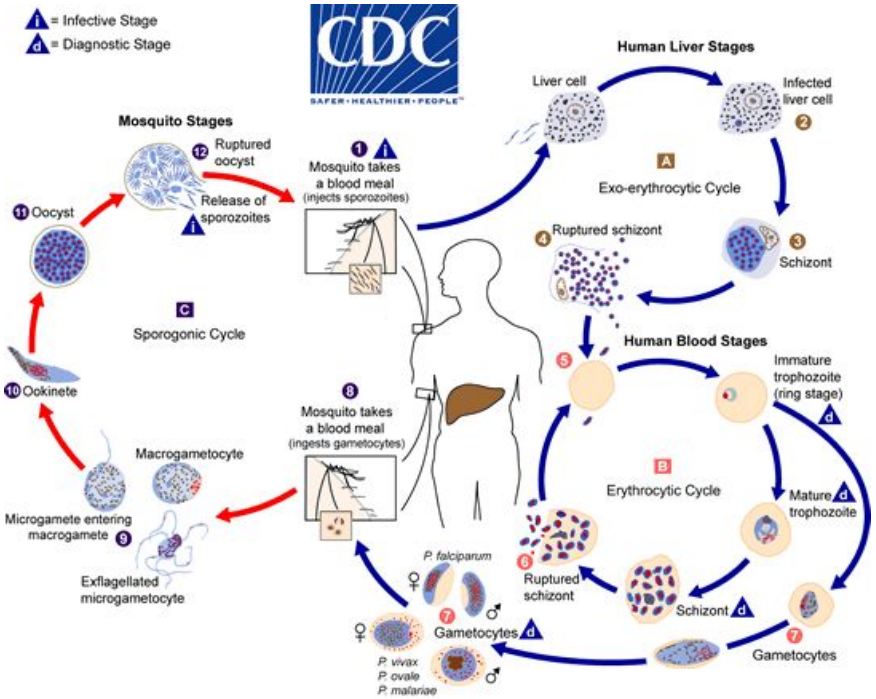
1: Most common cause especially illegal undocumented workers
2: They are the cause of indigenous cases especially during winter even though its only a minor percentage

Plasmodium Parasites

Five protozoan parasites that are known to affect humans:

Plasmodium falciparum · **P. vivax**[1] · **P. ovale** · **P. malariae** · **P. knowlesi**[2]

Mode of transmission and lifecycle:



- **MAINLY Vector** (female Anopheles mosquitoes)
- Blood (injection/transfusion of contaminated blood)
- **Congenital (rare)**

Recall from Microbiology
Explanation for the picture:
1. Malaria is mainly carried by **female anopheles mosquito.**
2. The infected mosquito will **bite and inject sporozoites** from it salivary gland into the bloodstream of human
3. Which then will travel through blood until it reaches the liver and enter the hepatocytes where it will multiply asexually to form **merozoites inside the schizont (Exoerythrocytic schizont).**
4. When the **hepatic schizont rupture (clinical symptoms appear)** the merozoites will be released into blood, then it will enter the erythrocytes forming **immature trophozoites (ring stage)** which will have 2 pathways:
a. **First pathway:** It goes through the **erythrocytic cycle** starting from ring stage then into Mature trophozoites, then the merozoites will multiply inside the RBCs forming **schizont (Erythrocytic schizont**), which will rupture (hemolysis) and release the merozoites into the bloodstream (Clinical attack of malaria is due to this stage) and the cycle will repeat over and over again.
b. **Second pathway:** Some immature trophozoites will become **gametocytes (male and female)** those gametocytes will be ingested by another mosquito; in the mosquito:
i. There are Micro(Male) and Macro(Female) gametocytes, the microgametocytes will enter into the macrogametocytes in which they will form Ookinete then it will develop into Oocyst which will rupture releasing **sporozoites** in mosquito, then the cycle will go over and over again.

1- India, Afghanistan
2- Documented in South east Asia.

History and Clinical features OSCE

Symptoms are not specific

- **Paroxysms of:**
Chills/rigors followed by fever, sweats
- A pattern might develop (i.e., fever occur every 2-3 days)
- Headache, weakness, muscle and joint pain.

Common

Less common

Anorexia

Nausea, vomiting

Diarrhoea

Abdominal pain

- ↑ **suspicion index** (e.g., **travel history**); the presentation within 3 months of exposure (P. falciparum) or up to 1 year (P. vivax & ovale).
- **In children** → influenza-like respiratory symptoms. (Atypical presentation)

History and Risk Factors

- **Travel history** is key in patients presenting in non-endemic countries. If positive, history of prophylaxis must be obtained. Must ask because some patients maybe asymptomatic
- **Settled migrants.**
- **Low host immunity.**
- **Pregnancy.**
- Children aged less than five years.
- Elderly.

Physical examination

- **Bedside examination might reveal the following signs:**
  - Hepatosplenomegaly due to 1- liver stage + Human blood stage 2-Hemolysis-> anemia -> pale
  - Anaemia signs (e.g., pallor)

★ **It is important to pick up the complications of severe malaria such as: because treatment differs in severe cases**

  - Confusion/altered level of consciousness
  - Seizures
  - Hypotension
  - Oliguria/anuria
  - Jaundice
  - Respiratory distress

Investigations OSCE

Laboratory

1. **Rapid diagnostic test (RDT)**[1]
2. **Light Microscopy:**[2]
   Giemsa-stained blood smear; Thin film, thick film.
3. **Polymerase Chain Reaction (PCR)** large hospitals
3. **Loop-mediated Isothermal Amplification (LAMP)**[3]
   An emerging test

Other baseline tests

- **Full blood count (FBC)** for anemia or hemolysis people with sickle cell anemia tend to be immune to Malaria
- **Clotting profile**
- **Serum electrolytes**
- **Urea and creatinine (U&E)**
- **Liver function tests (LFTs)**
- **Blood glucose** Hypoglycemia due to chloroquine- resistance
- **Urinalysis**
- **Arterial blood gas (ABG)** you might see Lactic acidosis

Community diagnosis

Pre-elimination[4]	Eliminated	Epidemic-prone areas
Areas with advanced malaria control	**Areas where malaria has been eliminated**	
- Universal access to diagnostic tests/ capabilities. - **Surveillance**/mapping. - Focused **screening** (e.g., those who present with danger signs) and treatment (e.g., active case strategy in Oman).	- Prevent re-introduction. - Considerable resources are still needed. - Different strategies (e.g., border control, active case management). - Maintain high-quality diagnosis	- Vigilance (e.g., investigations of unusual increase in cases with fever) **- Field surveys with RDTs**

Which of the following preventive measures is included in the malaria control program ? Case Management

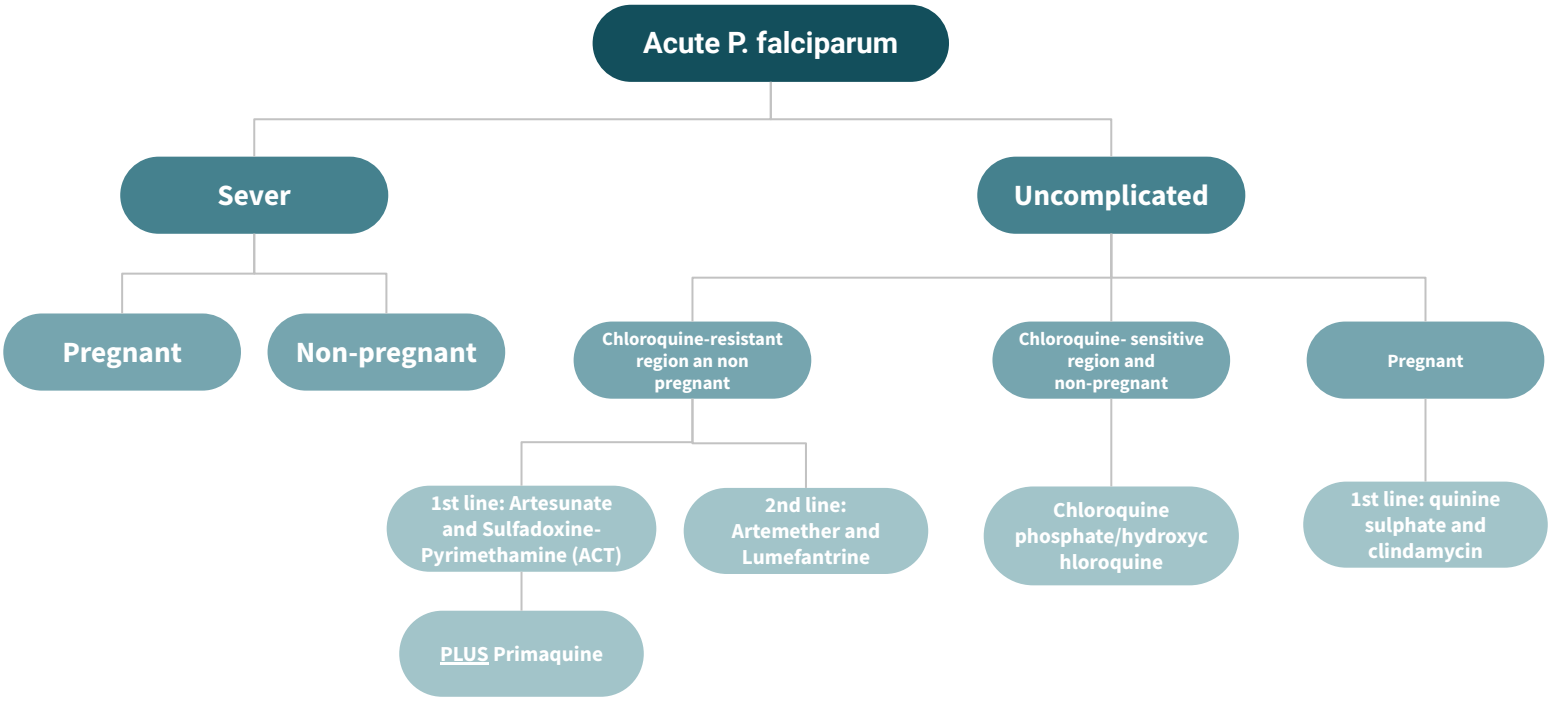
1: Anyone can do it, but not specific and you can't tell the type of Protozoa. It is used in community diagnosis (because it is rapid) where you scan a lot of people.
2: It's specific. It tells you the type of Protozoa but someone has to be very skilled in order to count on it as diagnostic (picture it as an Ultrasound where it's operator dependent)
3: New diagnostic tool it's still under development but promising because it's cheap and specific
4: Saudi is in this stage

Management

Treatment will depend on:

- Geographical area (sensitivity V resistance)
- The infecting species (falciparum V the rest)
- Blood smear appearance (parasite load; stage)
- Clinical status (acute v ongoing; uncomplicated v severe; pregnancy)

Treatment algorithm: an example ★



- Saudi Arabia is **considered as a chloroquine-resistant** area as the first case of resistance was reported in the late 1980s, therefore, Artemisinin Combination Therapy (ACT) is recommended (MOH 2019).
- Treatment of malaria in pregnancy must be discussed with an infectious diseases specialist.

★ **Primaquine is contraindicated in:**

G6PG deficiency[1] ↕ Infants <6m ↕ Pregnancy ↕ Hypersensitivity ↕ lactating mothers for babies <6m

1- The evidence is still uncertain if patients with P. Falciparum infection and glucose-6-phosphate dehydrogenase deficiency (G6PD) should not be given primaquine (BMJ 2020).

Management

Treatment failure → Antimalarial drug resistance

behaviour — Health workers / patients' behaviour (incorrect dose; poor compliance)

National policy — Poor national policy (drug quality; distribution)

Parasite — Parasite resistance

Three species known for resistance: P. falciparum, vivax and malariae.

Resistance to one drug confers resistance to others **(cross-resistance)** which leads to multidrug resistance

Resistance (gene mutations):

- **Complete:**
  - Survival / multiplication of malaria despite adequate treatment.
- **Partial:**
  - Delayed clearance or incomplete recovery.

The main cause of resistance is gene mutations

Incubation period for each organism

	Prepatent period	Incubation period
	Time between infective bite and **detection** of the parasite in a blood smear	Time between infective bite and **onset of clinical symptoms**
P. falciparum	6-12 days	9-14 days
P. vivax[1]	8-12 days	12-18 days
P. ovale	8-12 days	12-18 days
P. malariae	12-16 days	**18-40 days**

- **Period of communicability:**
  - Humans may infect mosquitoes as long as infective gametocytes are present in the blood.
  - Anopheles mosquitoes remains infective for life.

1- **Some strains of P. vivax, may have an IP of 8-10 months or longer**
Transfusion associated malaria has a shorter example IP.

Malaria Control

WHO efforts in malaria control (vision 2030)

VISION – A WORLD FREE OF MALARIA

GOALS	MILESTONES		TARGETS
	2020	2025	2030
1. Reduce malaria mortality rates globally compared with 2015	At least 40%	At least 75%	At least 90%
2. Reduce malaria case incidence globally compared with 2015	At least 40%	At least 75%	At least 90%
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least 10 countries	At least 20 countries	At least 35 countries
4. Prevent re-establishment of malaria in all countries that are malaria-free	Re-establishment prevented	Re-establishment prevented	Re-establishment prevented

Global technical strategy "GTS" (2016-2030)

STRATEGIC FRAMEWORK

– comprising three major pillars, with two supporting elements: (1) innovation and research and (2) a strong enabling environment

Maximize impact of today's life-saving tools

- **Pillar 1.** Ensure universal access to malaria prevention, diagnosis and treatment
- **Pillar 2.** Accelerate efforts towards elimination and attainment of malaria-free status
- **Pillar 3.** Transform malaria surveillance into a core intervention

Supporting element 1. Harnessing innovation and expanding research

- Basic research to foster innovation and the development of new and improved tools
- Implementation research to optimize impact and cost–effectiveness of existing tools and strategies
- Action to facilitate rapid uptake of new tools, interventions and strategies

Supporting element 2. Strengthening the enabling environment

- Strong political and financial commitments
- Multisectoral approaches, and cross-border and regional collaborations
- Stewardship of entire heath system including the private sector, with strong regulatory support
- Capacity development for both effective programme management and research

Malaria Control ★

Global measures to combat malaria: Pillar 1

Pilar 1: Ensure **universal access** to malaria prevention, diagnosis and treatment

1- Vector control

- Maximise the impact of vector control
- Maintain adequate **entomological** surveillance and monitoring
- Manage insecticide resistance and residual transmission
- Strengthen capacity for evidence- driven vector control
- Implement malaria vector control in the context of integrated vector management

2- Chemo-prevention

subtherapeutic doses of malaria treatment for prophylaxis

- Expand preventive treatment to prevent disease in the most vulnerable groups.
- Protect all non-immune travellers and migrants.

Example: Someone plans on traveling to an endemic chloroquine- resistant country? Doxycycline (before/during/after travel)

3- Diagnostic testing and treatment

- Ensure universal diagnostic testing of all suspected malaria cases.
- Provide quality assured treatment to all patients.
- Monitor safety and efficacy of antimalarial medicines and manage antimalarial drug resistance.
- Contain antimalarial drug resistance.
- Eliminate falciparum malaria from the Greater Mekong subregion.
- Remove all inappropriate antimalarial medicines from market.
- All countries should aim to eliminate malaria.
- Scale up community based diagnostic testing and treatment.

- All suspected cases must be confirmed first before given treatment. If treatment failure is > 10% , first line therapy is reviewed (every 2 years, countries review their malaria health policies)
- Use multiple drugs (combination) to avoid resistance

Malaria Control ★

Global measures to combat malaria: Pillar 2 & 3

Pillar 2: accelerate **efforts towards elimination** and attainment of malaria-free status

- Refocus programmes
- **Enact legislation**
- Renew political commitment and deepen regional collaboration
- Reduce the number of undetected infections
- Implement targeted malaria vector control
- Prevent re-establishment of local malaria transmission
- Implement transmission-blocking chemotherapy in high transmission/resistance cases
- Detect all infections to attain elimination and prevent reestablishment
- Use of medicines to reduce the parasite pool
- **Devise P. vivax-specific strategies** the problem is that it can live in multi environments so it's very resistant
- Use **surveillance** as an intervention in elimination programs

Pillar 3: transform malaria surveillance into a core intervention

- **Surveillance in areas of high** (focus on no. of deaths and cases) **and low** (focus on high risk groups) **transmission.**
- Surveillance in areas targeted for elimination of malaria
- **Invest** in routine information systems
- Collect necessary data for understanding disease trends and overall programme performance
- Develop national strategic plans that take into account the epidemiology and heterogeneity of malaria in a country
- Monitor the implementation of national malaria strategic plans at regular intervals
- **Ensure the surveillance system is monitored**

Supporting element 1: harnessing innovation and expanding **research**

- Vector control
- Diagnostic testing and treatment
- Malaria vaccines
- Surveillance
- Elimination

Supporting element 2: strengthening the enabling environment

- Increase international and domestic financing
- Ensure robust health sector response
- Strengthen health workforce and malaria expert base
- Ensure the sustainability of malaria responses
- Improve government stewardship
- Strengthen multisectoral collaboration
- Encourage private sector participation
- Empower communities and engage with non-governmental organisation

Cases

Case 1

A child aged 3 years is brought in for fever over the past 24 h. The father reports no cough or diarrhoea.
Physical examination shows a temperature of 38.6 °C but no other major sign.
RDT is negative.
(1) What is your diagnosis?
(2) What advice do you give to the father, and what treatment do you prescribe?

Non-specific fever (without danger signs)
1) Diagnosis: non-specific fever or **non-malaria** fever or flu-like syndrome
2) Reassure the father that his child does not have malaria. Tell him to bring the child again if the fever persists or if a new problem appears. Treat the child with an antipyretic only.
Take home message: **RDT is negative → No malaria → No antimalarial treatment**

Case 2

An infant aged 11 months is brought to a dispensary for fever over the past 48 h. The mother reports difficulty in breastfeeding since the previous day and one episode of convulsion.
Physical examination shows a temperature of 38.6 °C and slight drowsiness but no other major sign.
Explain the actions you would take, one by one.

- **Difficulty to suck, convulsion, drowsiness** = **Danger signs**
- Do not lose time by asking for malaria tests; they will be done at the hospital.
- Immediately prescribe an antimalarial and an antibiotic treatment (and antipyretic)
- Refer the infant urgently to hospital

Take home message: **Danger signs antimalarial+antibiotic + immediate referral**

Exercise:
Identify key factors and common clinical Features

A 42-year-old **Nigerian** woman presents to her primary care physician with a 2-day history of **fever, chills, and sweats with associated headache and myalgia. She is febrile** (38.6C [101.4 F]) and **tachycardic**, but examination is otherwise unremarkable. A presumptive diagnosis of influenza is made, and she is advised to return if she does not improve. Two days later she presents to the **emergency department** with similar symptoms and **frequent vomiting**. On examination she **appears ill**, with a temperature of 38.8°C (101.8'F), pulse rate **120 beats per minute**, blood pressure 105/60 mmHg, and **mild jaundice**. Further history reveals that she recently **visited family in Nigeria for 2 months, returning 1 week before presentation**. She **did not** take malaria prophylaxis.

Quiz

MCQ

1- Sporozoites when injected into the human skin it migrates to?

A- Hepatocytes. B- Intestinal wall. C- Macrophages. D- Lymphocytes.

2- What is the main organ affected in malaria infection?

A- Liver. B- kidney. C- RBCs. D- intestine.

3- which one of the following has immunity against malaria:

A- sickle cell trait B- microcytic anemia C- G6PG deficiency D- children less than 6

4- the main way to reduce malaria transmission at a community is

A- human control B- vector control C- environmental control

5- You work in prevention of malaria in west Africa, what is the best prevention?

A- Mass vaccination B- Use insecticides in beds and crops C- use spray nets D- Drinking a lot of orange juice

6- What is the main mode of transmission in malaria?

A- Blood Transfusion B- Animal bite C- TransPlacental D- Vector borne

Answers

Q1	Q2	Q3	Q4	Q5	Q6
A	C	A	B	C	D

Thank You and Good Luck

Community Medicine
438

Team Leaders:

Lama AlAssiri | Mohammed AlHuqbani | Ibrahim AlDakhil

Team Members:

- Lama AlZamil
- Leen AlMazroa
- Muneera AlKhorayef
- Norah AlMazrou
- Nouf Alhussaini
- Rema AlMutawa
- Sara AlAbdulkareem
- Sedra Elsirawani
- Wejdan Alnufaie
- Abdulrahman Alhawas
- Abdulrahman Shadid
- Abdullah Aldawood
- Abdullah Shadid
- Alwaleed Alsaleh
- Bader Alshehri
- Bassam Alkhuwaiter
- Faisal Alqifari
- Hameed M. Humaid
- Khalid Alkhani
- Meshari Alzeer
- Mohannad Makkawi
- Nayef Alsaber
- Omar Aldosari
- Omar Alghadir
- Zyad Aldosari